19. The complementary compound of claim 17 wherein the critical region is the G3:U70 base pair.

21. The complementary compound of claim 11 wherein the compound is a nucleic acid and the compound is synthesized *in vivo* from a retroviral vector.

REMARKS

Status of Claims

Claims 1 and 3-21 are pending. Claims 1 and 3-21 are on appeal. A clean and marked up copy of all of the pending claims as amended is attached to this Response as an appendix.

Enablement

The Board's decision, mailed on April 30, 2001, held that, while the factors relied on by the examiner are relevant in determining enablement by the specification, they are insufficient to establish that the experimentation required to practice the claimed invention is undue. The examiner's rejection of claims 1 and 3 through 21 for lack of enablement under 35 U.S.C. § 112, first paragraph, was reversed.

Double Patenting

In response to the Board's affirmation of the provisional double patenting rejections for claims 11, 12 and 17 through 19 under 35 U.S.C. § 101 and claims 1, 3 through 6, 8 through 10, 13 through 16, 20 and 21 under the judicially-created doctrine of obviousness-type double patenting, the assignee, Massachusetts Institute of Technology, submits an executed terminal disclaimer to obviate the provisional double patenting rejections.

NEW GROUND OF REJECTION

Written Description

Under the provisions of 37 C.F.R. § 1.196(b), the Board has entered a new ground of rejection under the first paragraph of 35 U.S.C. § 112 on the basis that the specification fails to provide an adequate written description for claims 11 through 13, 17 through 19 and 21.

Appellant has amended base claim 11, and claims dependent thereon, to more clearly define the composition as a compound that is complementary to the target RNA sequence comprising hydrogen bond donor and acceptor sites. Lines 29-17, bridging pages 38 and 39, for example, provide support for these amendments.

The Federal Circuit has defined what constitutes conception of a compound and characteristics that distinguish a chemical compound composition from others by stating, "....conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it." *Amgen*, 927 F.2d at 1206, 18 USPQ 2d at 1021. Furthermore the court has stated that in order to satisfy the written description requirement, "the applicant need not describe the subject matter claimed in exact terms. However, the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." *Monsanto Co. v. Mycogen Plant Science*, Inc., 61 F.Supp.2d 133, 188 (D.Del. Aug 18, 1999).

Appellant respectfully submits that the specification describes the structure of the claimed compound by illustrating the chemical properties (hydrogen bond acceptor and donor sites arranged specifically) and method of preparation (first, determining the target RNA sequence and second, preparing the compound accordingly) of the compound. This description distinguishes the composition based on the claimed interaction with a critical region in the minor groove of the target RNA. Although the compounds may be organic, inorganic, proteins, or even nucleic acids, specific binding is achieved through complementary interactions (page 38 of the specification, lines 24-31). These interactions are dependent upon hydrogen bonding (lines 29-17, bridging pages 38 and 39). Therefore, in order for the compound to bind to the target RNA, hydrogen bond donor sites, hydrogen bond acceptor sites, and chemical side groups, have to be in the correct spatial location, orientation, and have the correct charge. One of skill in the art would realize that it is this arrangement that defines the structure of the compound. "Complementary" defines the structure of the compound. Complementary compounds are limited by the sequence of the RNA target molecule. Given the minor groove sequence of the RNA to be targeted, the arrangement of possible hydrogen bonds to be utilized by the compound is defined, therefore limiting the structure of the compound.

As stated in M.P.E.P. § 2173.05(t), which describes the standard to be applied to compounds and compositions, "a compound of unknown structure may be claimed by a combination of physical and chemical characteristics." See *Ex parte Brian*, 118 USPQ 242 (Bd. App. 1958). M.P.E.P. § 2173.05(t) further states that "a compound may also be claimed in terms of the process by which it is made without raising an issue of indefiniteness." It is important to

note that only *after* obtaining the correct target RNA sequence, can the claimed compound and its structure be elucidated. This, however, is routine to those skilled in the art. The structural features common to the members of the claimed genus can only be determined once the hydrogen bonding arrangement of the target sequence is derived. Once the RNA sequence is derived, the minor groove structure can be easily inserted into any number of commercially available computer programs and the structural features of the compound determined. The structure of the compound is clearly limited based on the requirement for it to be complementary to the RNA sequence.

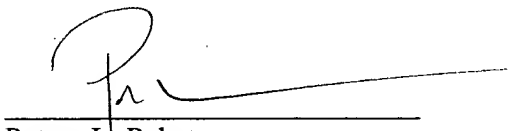
The complementary nature of the compound of base claim 11 distinguishes the claimed compound from others. Compounds that bind a RNA in the minor groove would not necessarily have the requisite correct charge and spatial orientation of the potential hydrogen bond donors and acceptors to be specific for presentation and binding to the targeted critical region of a RNA molecule. While most, if not all, compounds that bind RNA do have hydrogen bonding sites, only a few will have the necessary pattern of sites to be utilized specifically by the targeted critical region. The identification of the critical region within the minor groove by a combination of primary, secondary and tertiary structure analysis, as recited in claim 11, is required for the determination of the structure of the compound. Therefore the structural features common to the claimed compound, as defined by the term "complementary" and by containing the requisite hydrogen bonding acceptor and donor sites, are clearly described.

The specification also discloses other relevant information and identifying characteristics sufficient to describe the claimed invention. One of skill in the art would be able to predict with

a reasonable degree of confidence the structure of the claimed complementary compound from the recitation of its function. It is well established that the written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. The appellant respectfully submits that this correlation has been established as described above. The hydrogen bonding pattern of the compound defines the structure of the compound, however, this defining characteristic is at the mercy of RNA analysis as described in base claim 11.

Allowance of claims 1 and 3-21 is respectfully solicited.

Respectfully submitted,



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Certificate of Mailing Under 37 C.F.R. § 1.8(a)

I hereby certify that this Response to Decision by Board of Patent Appeals and Interferences, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Board of Patent Appeals and Interferences, Washington, D.C. 20231.

Aisha Wyatt

Date: July 2, 2001

Marked Up Version of Amended Claims

Pursuant to 37 C.F.R. § 1.121(c)(1)(ii)

1. A method for designing a compound specifically inhibiting targeted ribonucleic acid function comprising the steps of:

(a) determining the nucleotide sequence in the targeted ribonucleic acid that is critical to function;

(b) determining the secondary structure of the region of the targeted ribonucleic acid in which the critical site is located;

(c) determining the three-dimensional structure of the targeted RNA, including the position of the critical site relative to the major and minor grooves;

(d) determining the sequence of nucleotides and structure flanking the critical site in the targeted ribonucleic acid that is specific to the critical region of the ribonucleic acid to be inhibited and within the minor groove; and

(e) synthesizing a compound that will bind specifically to the critical site within the minor groove of the targeted ribonucleic acid thereby inhibiting targeted ribonucleic acid function.

3. The method of claim 1 wherein the ribonucleic acid is selected from the group consisting of mRNA, rRNA, tRNA and viral RNA.

4. The method of claim 1 wherein inhibition of targeted ribonucleic acid function inhibits protein synthesis.

5. The method of claim 4 wherein protein synthesis is inhibited in cells selected from the group consisting of tumor cells, virally infected cells, and bacterial cells.

6. The method of claim 1 wherein the three-dimensional structure is modeled using sequences of the RNA and calculating the minimum energies for these structures.

7. The method of claim 1 wherein the critical region of the targeted ribonucleic acid is determined by mutation of regions of the targeted RNA and comparison of the function of the mutated RNA with the original RNA, wherein mutations that result in mutant RNA having altered function indicate that the site of mutation is a critical site.

8. The method of claim 1 wherein the targeted RNA is a tRNA, wherein the critical region of the tRNA is determined by site directed mutation of the tRNA and analysis of the function of the mutated tRNA.

9. The method of claim 1 further comprising determining an effective amount of the compound and combining the compound with a pharmaceutical carrier.

10. The method of claim 9 wherein the carrier is selected from the group consisting of pharmaceutically acceptable compositions for topical administration, pharmaceutically acceptable compositions for parenteral administration, pharmaceutically acceptable compositions for enteral administration, and combinations thereof.

11. A complementary compound comprising hydrogen bond donor and acceptor sites arranged to specifically bind [binding to] and inhibit [inhibiting] the function of a targeted RNA molecule, wherein the compound is specifically directed to and binds to a critical region of the RNA molecule, located within the minor groove of the RNA molecule, identified by a combination of the primary, secondary and tertiary structure of the critical region.

12. The complementary compound of claim 11 wherein the RNA is selected from the group consisting of mRNA, tRNA, rRNA, and viral RNA.

13. The complementary compound of claim 11 further comprising a pharmaceutically acceptable carrier selected from the group consisting of pharmaceutically acceptable compositions for topical administration, pharmaceutically acceptable compositions for parenteral administration, pharmaceutically acceptable compositions for enteral administration, and combinations thereof.

14. The method of claim 3 wherein the critical site is in the minor groove of the acceptor stem of a tRNA molecule.

15. The method of claim 14 wherein the tRNA molecule is $tRNA^{Ala}$.

16. The method of claim 15 wherein the critical site is the G3:U70 base pair.

17. The complementary compound of claim 12 wherein the compound binds to a critical region within the minor groove of the acceptor stem of a tRNA molecule.

18. The complementary compound of claim 17 wherein the tRNA molecule is $tRNA^{Ala}$.

19. The complementary compound of claim 17 wherein the critical region is the G3:U70 base pair.

20. The method of claim 1 wherein the compound is a nucleic acid and the compound is synthesized *in vivo* from a retroviral vector.

21. The complementary compound of claim 11 wherein the compound is a nucleic acid and the compound is synthesized *in vivo* from a retroviral vector.